INSTITUTE OF TROPICAL MEDICINE ANTWERP

DoxyPEP: what's new?

Thibaut Vanbaelen MD PhD

BREACH symposium 27/11/2025

Background

- Three RCTs demonstrated the efficacy of doxyPEP in reducing the incidence of
  - Chlamydia
  - Syphilis
  - (Gonorrhea)

  in MSM & TGW (PrEP users & PLHIV)
- No effect in cis-gender women in one RCT, probably due to low adherence
- There are concerns regarding adverse effects:
  - Antimicrobial resistance in STIs
  - Antimicrobial resistance in other bacteria
  - Effects on microbiome
  - …

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Doxy post-exposure prophylaxis for STI not endorsed by BREACH

De Scheerder M-A, Agnès Libois, Jens Van Praet and Chris Kenyon

After a debate at the BREACH symposium on November 30th 2023, a consensus was reached not to recommend the widespread use of DoxyPEP for the prevention of STI.

Doxycycline post exposure prophylaxis (Doxypep) is the intake of the antibiotic doxycycline 200 mg in prevention of sexually transmitted infections (STI). At least one dosis of the antibiotic is taken maximum 72 hours after the sexual contact. It is often taken in a context of risk sexual behaviour and in combination with PrEP as a prevention of HIV transmission.

DoxyPEP studies (Ipergay, doxyPEP, doxyVAC) showed efficacy to decrease the incidence of syphilis and chlamydia (and in some studies gonorrhea depending on the level of tetracycline resistance in gonorrhea) but the number of symptomatic infections was low or not reported.[1,2,3]The Belgian Gonoscreen study has shown little or no impact of screening for chlamydia and gonorrhea on the incidence of these infections in asymptomatic MSM taking PrEP.[4]

Antimicrobial resistance (AMR) is a huge concern in STI and other bacteria. Data on the use of doxycycline and resistance are very limited but some studies showed an increase in AMR.[5,6]

Considering that the number to treat to avoid a symptomatic infection with gonorrhea or chlamydia is probably very high, the considerable potential to select resistance in STIs and other bacterial species and the possibility of disrupting the microbiome, it's considered that potential individual benefits of doxyPEP is outweighed by the risks in men who have sex with men.

Further studies are required to measure the wider impact on AMR at an individual and population level.

Regular screening for syphilis and HIV stay crucial in people with high risk of STI acquisition.

In cases, where at an individual level, DoxyPEP is being prescribed, we encourage that this should be done in a medically supervised setting (HRC) and preferably in a research context (such as the SafeDoxyPEP Study at ITM) to generate more data on the impact of DoxyPEP on resistance and microbiome.

What's new since 2023?

- DoxyPEP implementation in several countries
- Real-world data on efficacy
- New data on
  - AMR in STIs
  - AMR in other bacteria
  - Effect on microbiome/resistome
  - Effect on syphilis serological response

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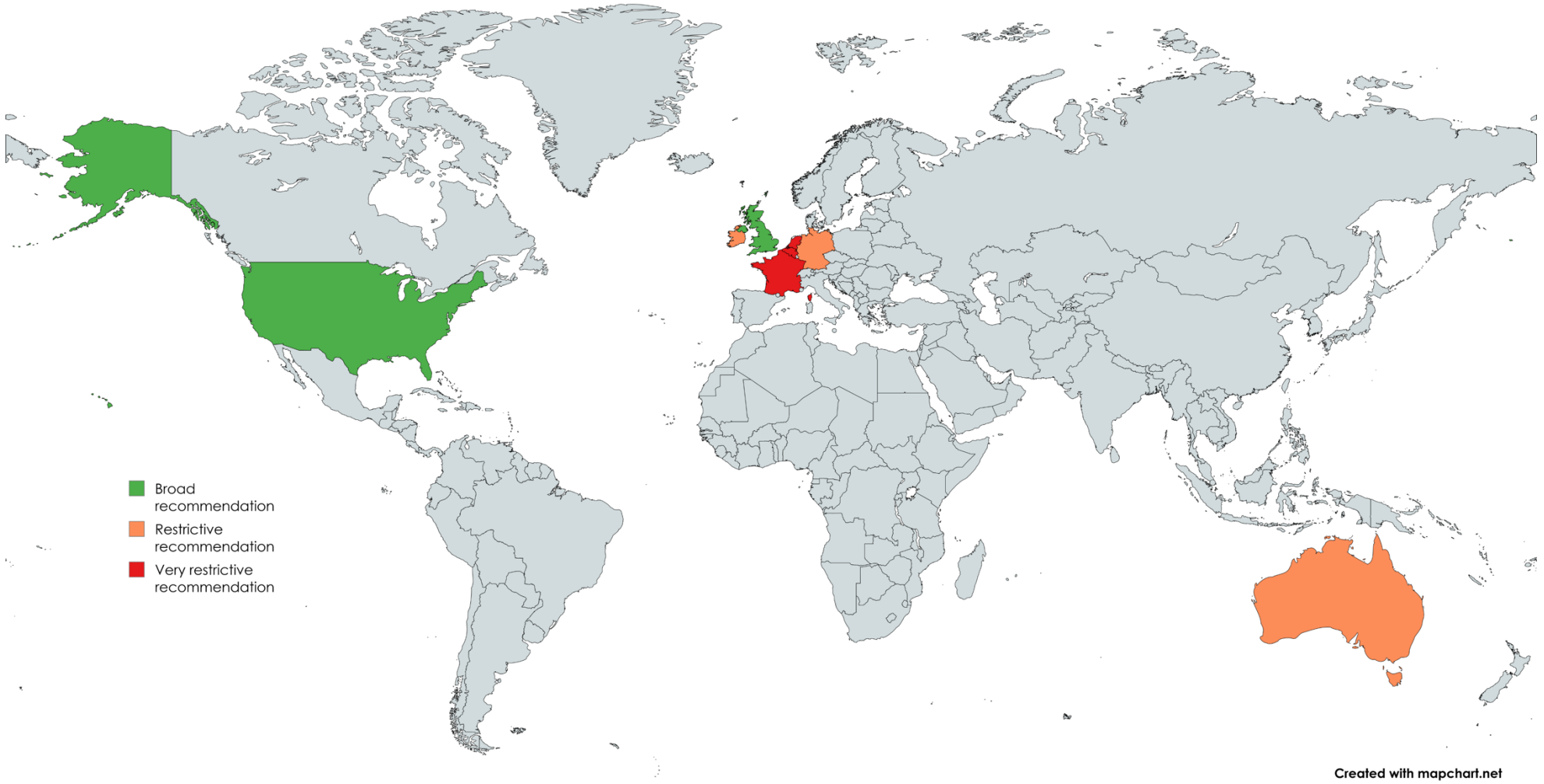
DoxyPEP implementation



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JAMA Internal Medicine | Original Investigation

Doxycycline Postexposure Prophylaxis and Bacterial Sexually Transmitted Infections Among Individuals Using HIV Preexposure Prophylaxis

Michael W. Traeger, PhD, MSc; Wendy A. Leyden, MPH; Jonathan E. Volk, MD; Michael J. Silverberg, PhD; Michael A. Horberg, MD; Teaniese L. Davis, PhD; Kenneth H. Mayer, MD; Douglas S. Krakower, MD; Jessica G. Young, PhD; Samuel M. Jenness, PhD; Julia L. Marcus, PhD

- Retrospective cohort study of 11 551 PrEP users in Northern California 2022-2023
- Examined electronic health record data to compare rates of bacterial STIs:
  - Dispensed vs not dispensed doxyPEP
  - Before and after starting doxyPEP

Figure 2. Trends in Quarterly Sexually Transmitted Infection Positivity From January 1, 2021, to December 31, 2023, Among HIV Preexposure Prophylaxis (PrEP) Users Dispensed and Not Dispensed Doxycycline Postexposure Prophylaxis (DoxyPEP) During the Study Period (N = 11 551)

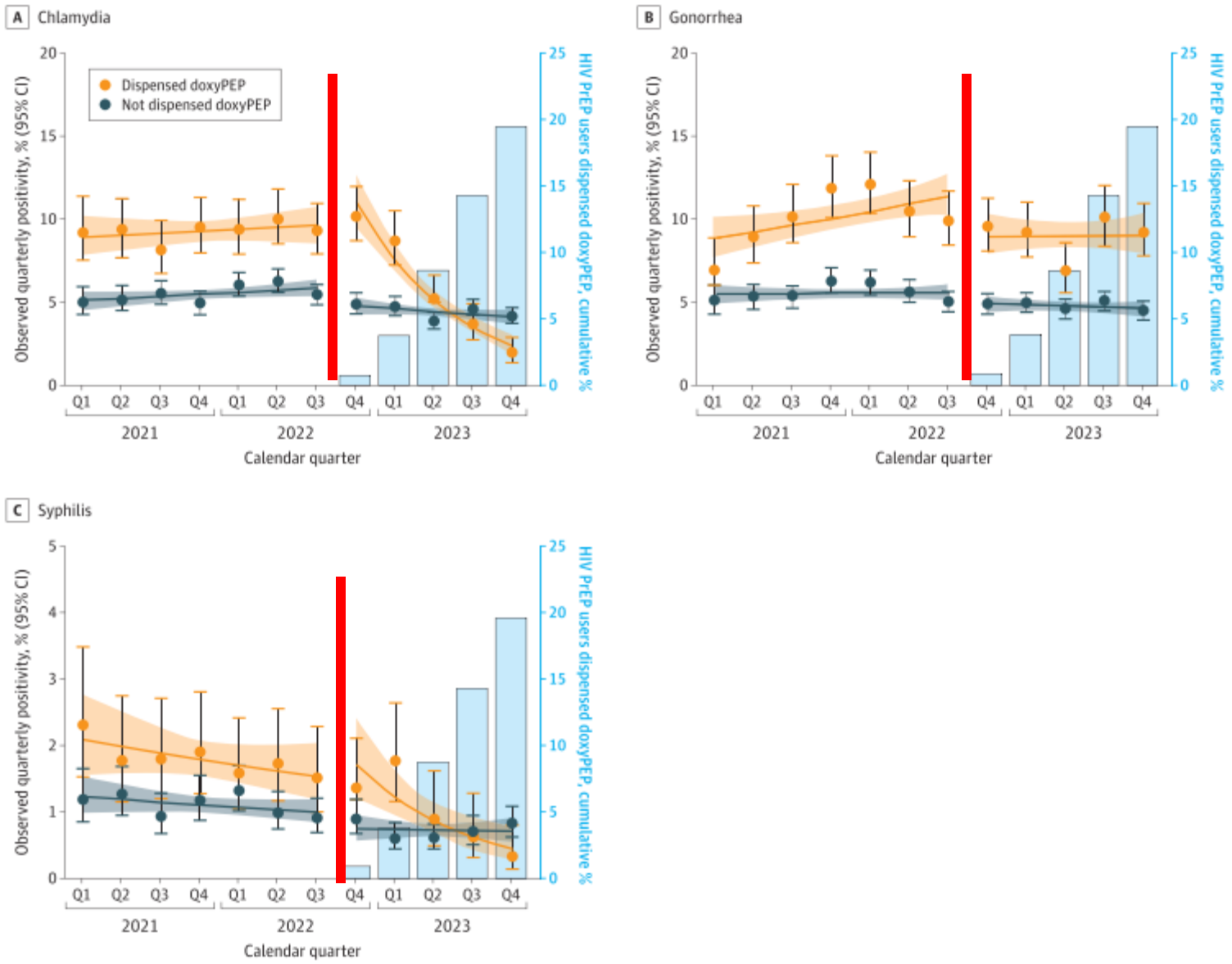
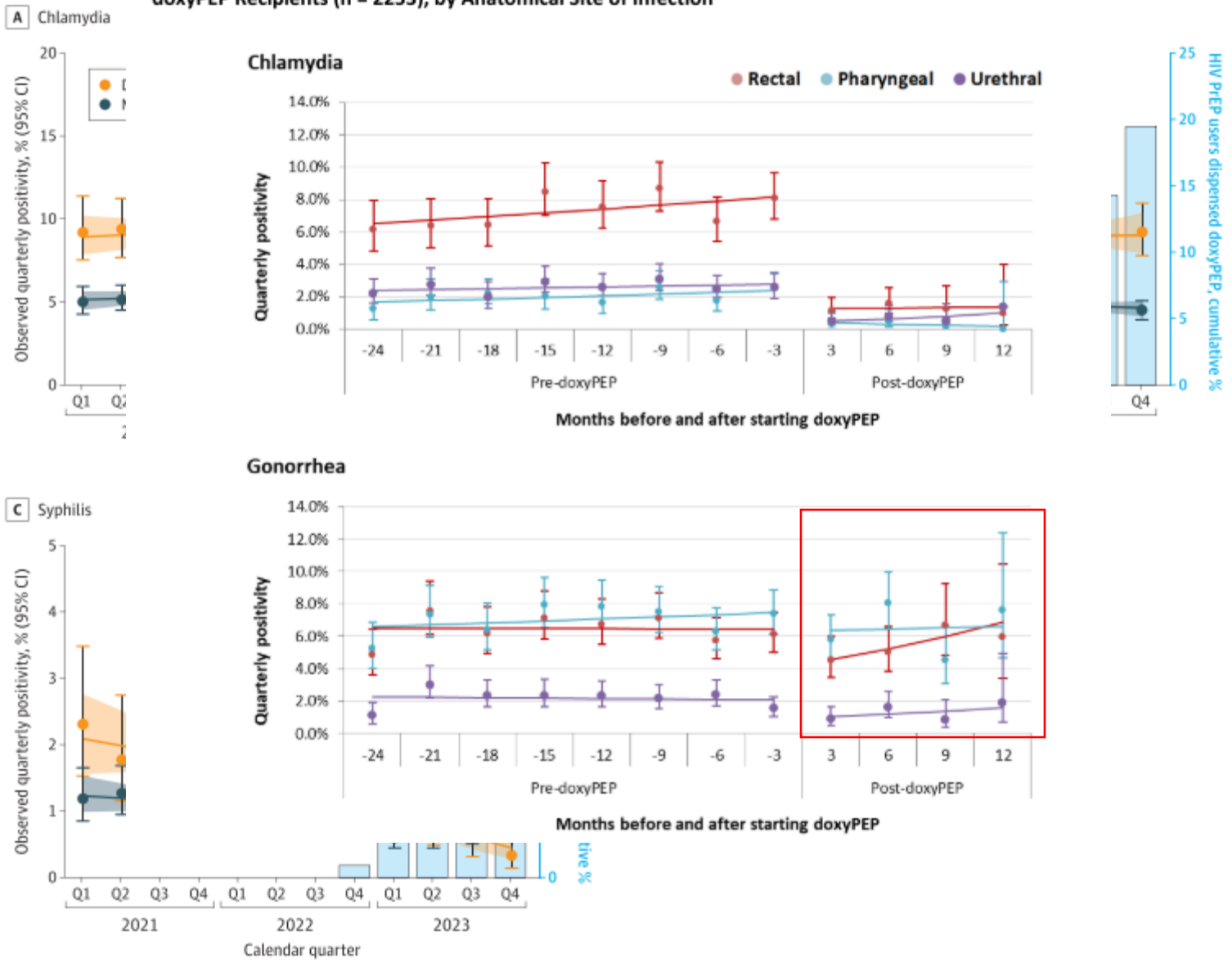


Figure 2. Trends in Quarterly Sexually Transmitted Infection Positivity From January 1, 2021, to December 31, 2023, Among HIV Preexposure Prophylaxis (P

eFigure 2. Quarterly Chlamydia and Gonorrhea Positivity From Before to After Starting doxyPEP Among doxyPEP Recipients (n = 2253), by Anatomical Site of Infection

: 11 551)



nature communications

Article

https://doi.org/10.1038/s41467-025-64261-w

Bacterial sexually transmitted infections and related antibiotic use among individuals eligible for doxycycline post-exposure prophylaxis in the United States

Received: 29 May 2025

Accepted: 10 September 2025

Anna M. Parker[1], Jennifer J. Chang[2], Ligong Chen[3], Laura M. King[1], Sandra I. McCoy[1,4], Joseph A. Lewnard[1,5,6,8] & Katia J. Bruxvoort[7,8]

- Modelling study based on healthcare data (2014-2019)
- Estimated the net increase in standardized tetracycline fill-days per incident STI diagnosis prevented by doxyPEP
- 38 543 person-years at risk among PrEP recipients
- 29 228 person-years among PLWH

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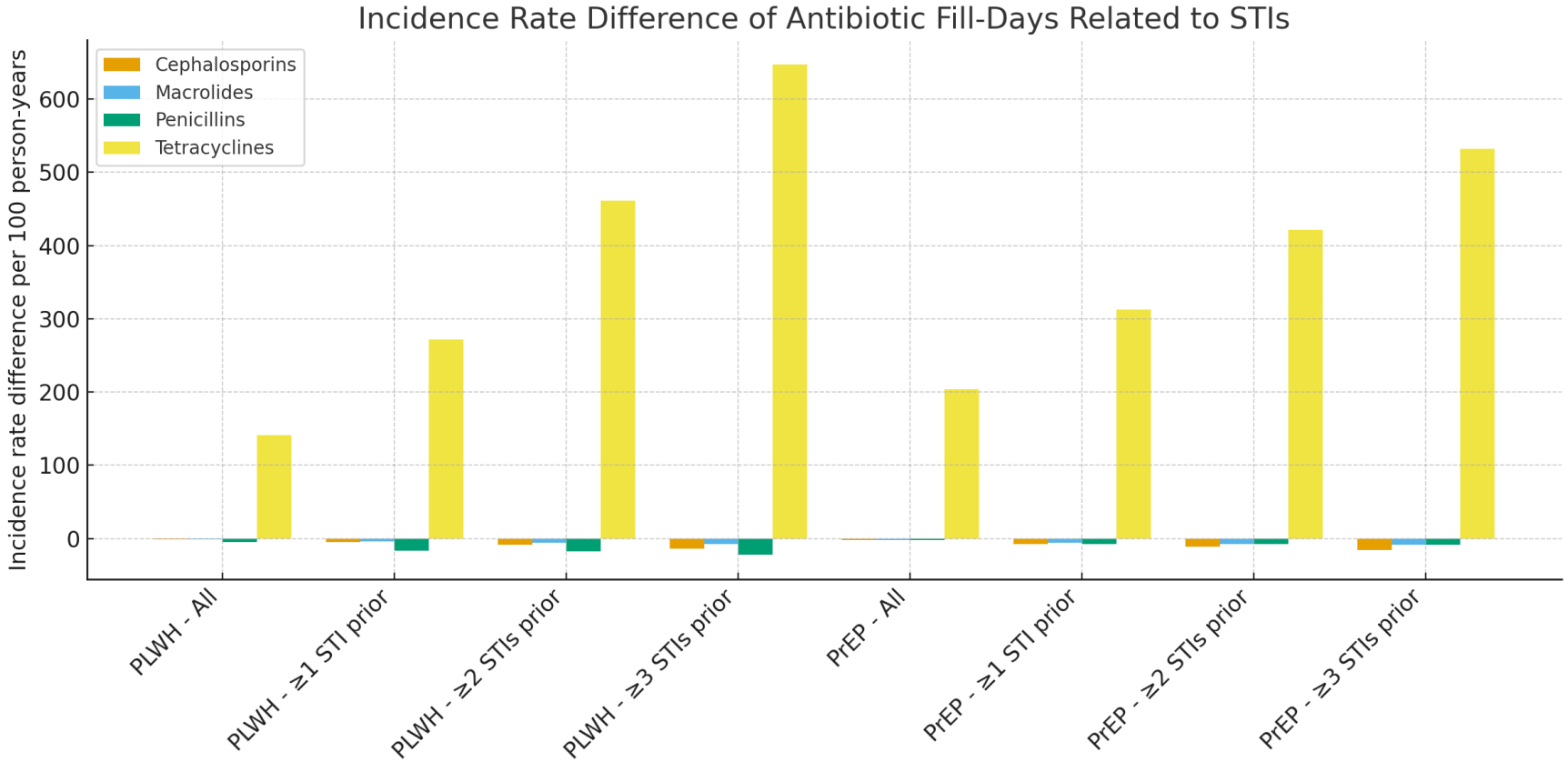

PLHIV

PrEP

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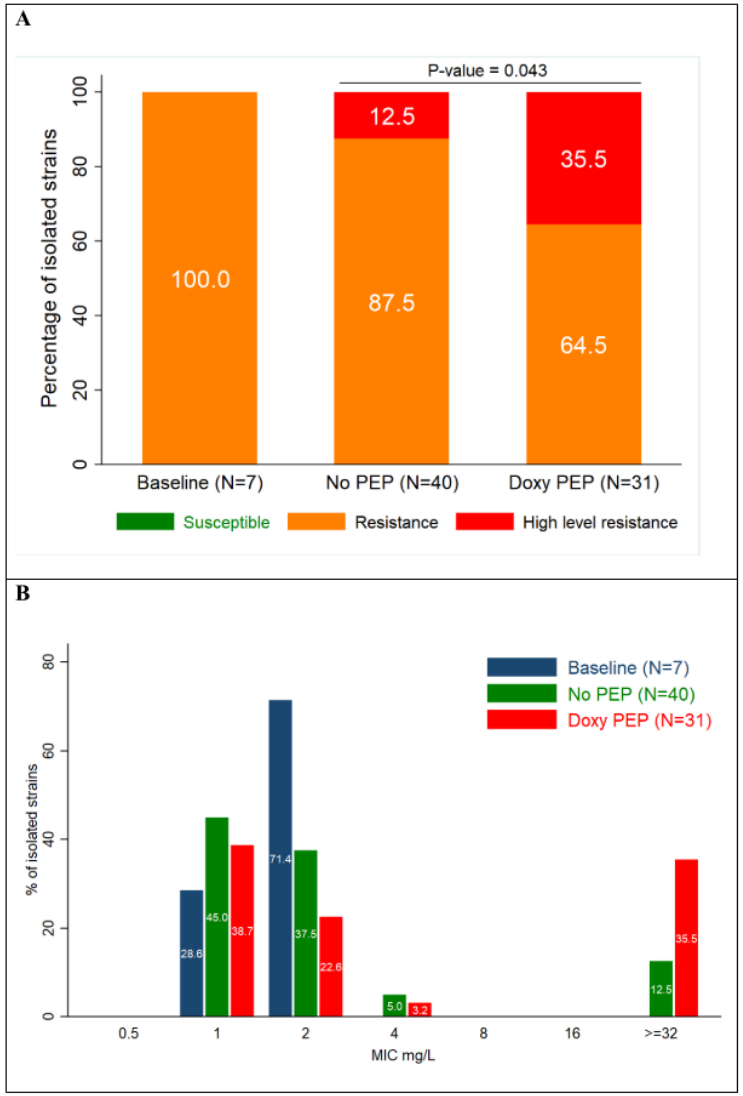
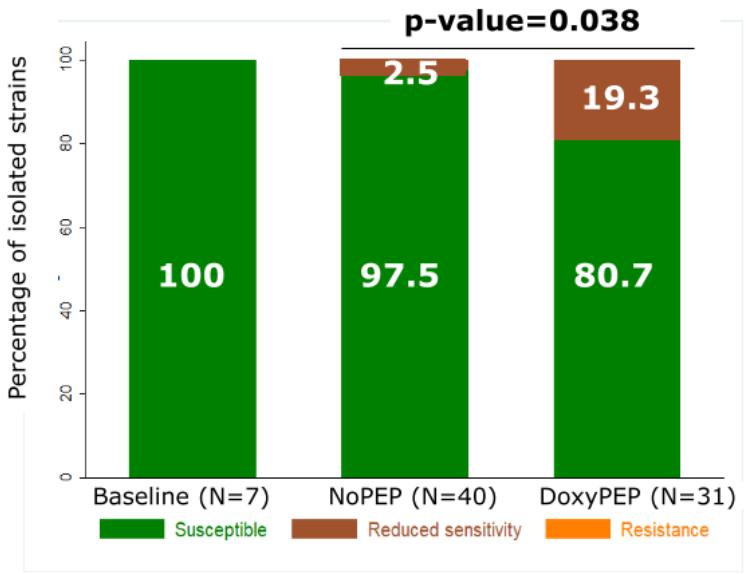
AMR in *N gonorrhoeae*

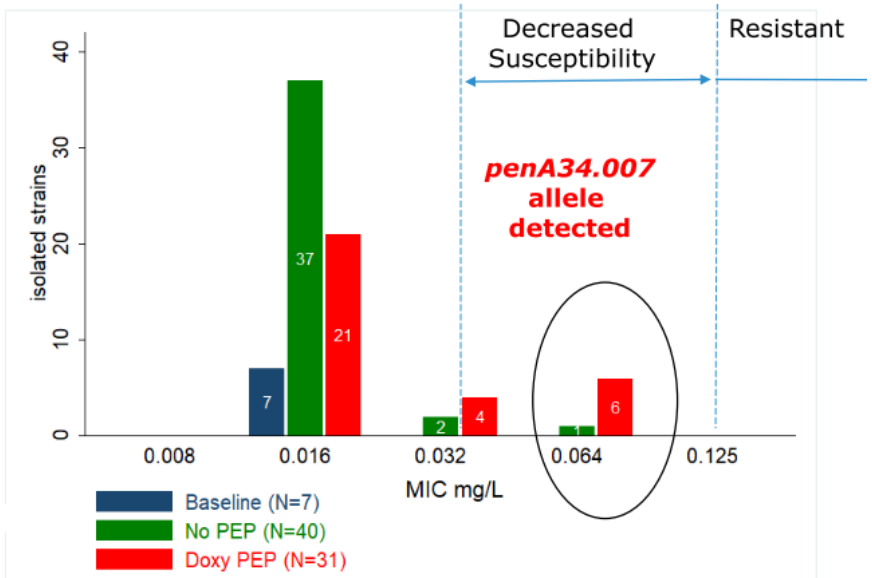


Decreased susceptibility to cefixime, MIC distribution

78 GC isolates

Isolates with Decreased Susceptibility to cefixime were more frequent in the doxyPEP arm.





Resistance: MIC>0.125 mg/L, Decreased susceptibility 0.125≤MIC>0.032 mg/L
www.eucast.org/clinical_breakpoints/

Berçot et al, IUSTI Europe 2025 & CID 2025

Figure 1. Prevalence of tetracycline resistance among MSM with NG, PHSKC Sexual Health Clinic, 2017–2024.

AMR in *N gonorrhoeae*

Soge et al, Clin Infect Dis, Volume 80, Issue 6, 15 June 2025, Pages 1188–1196, https://doi.org/10.1093/cid/ciaf089

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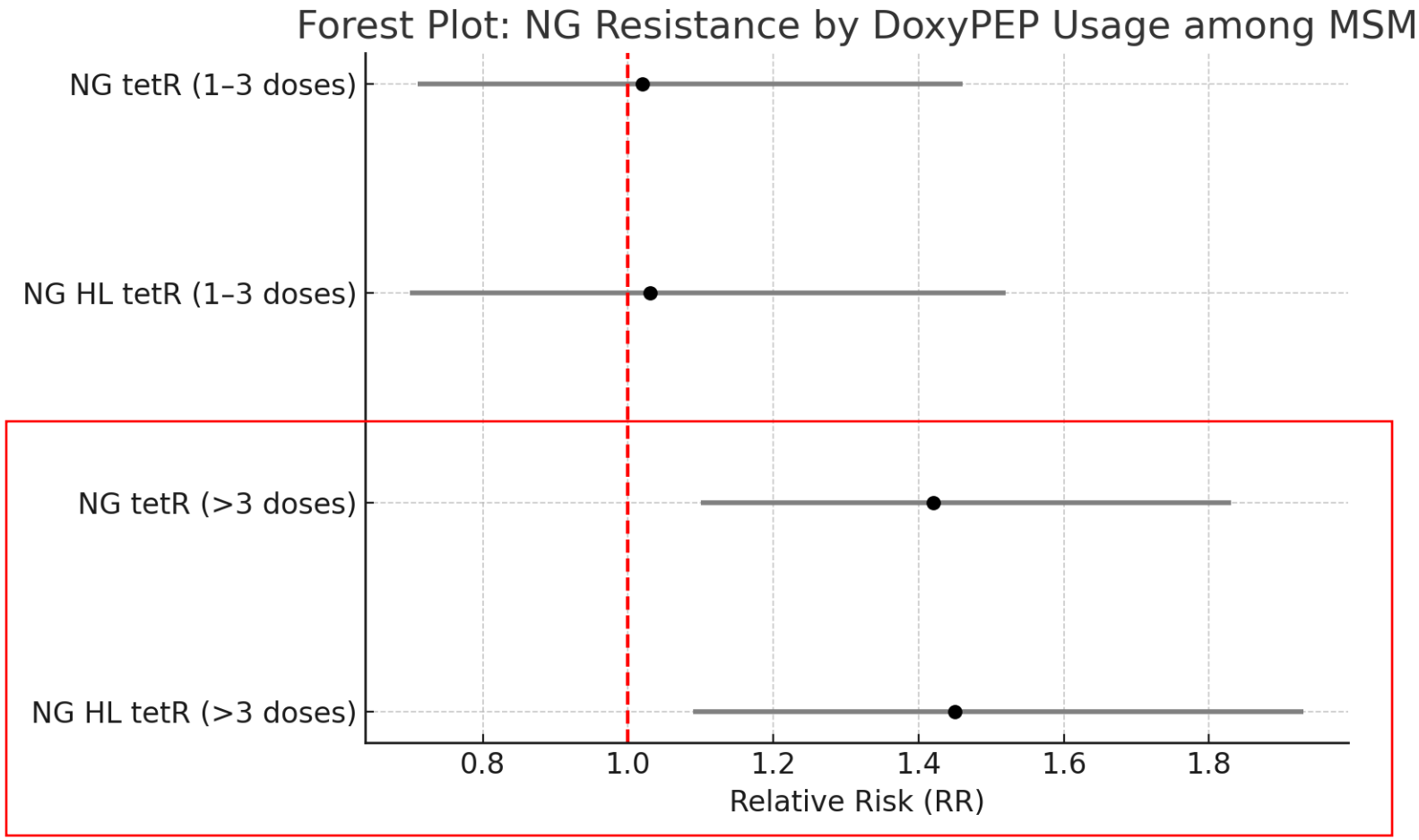

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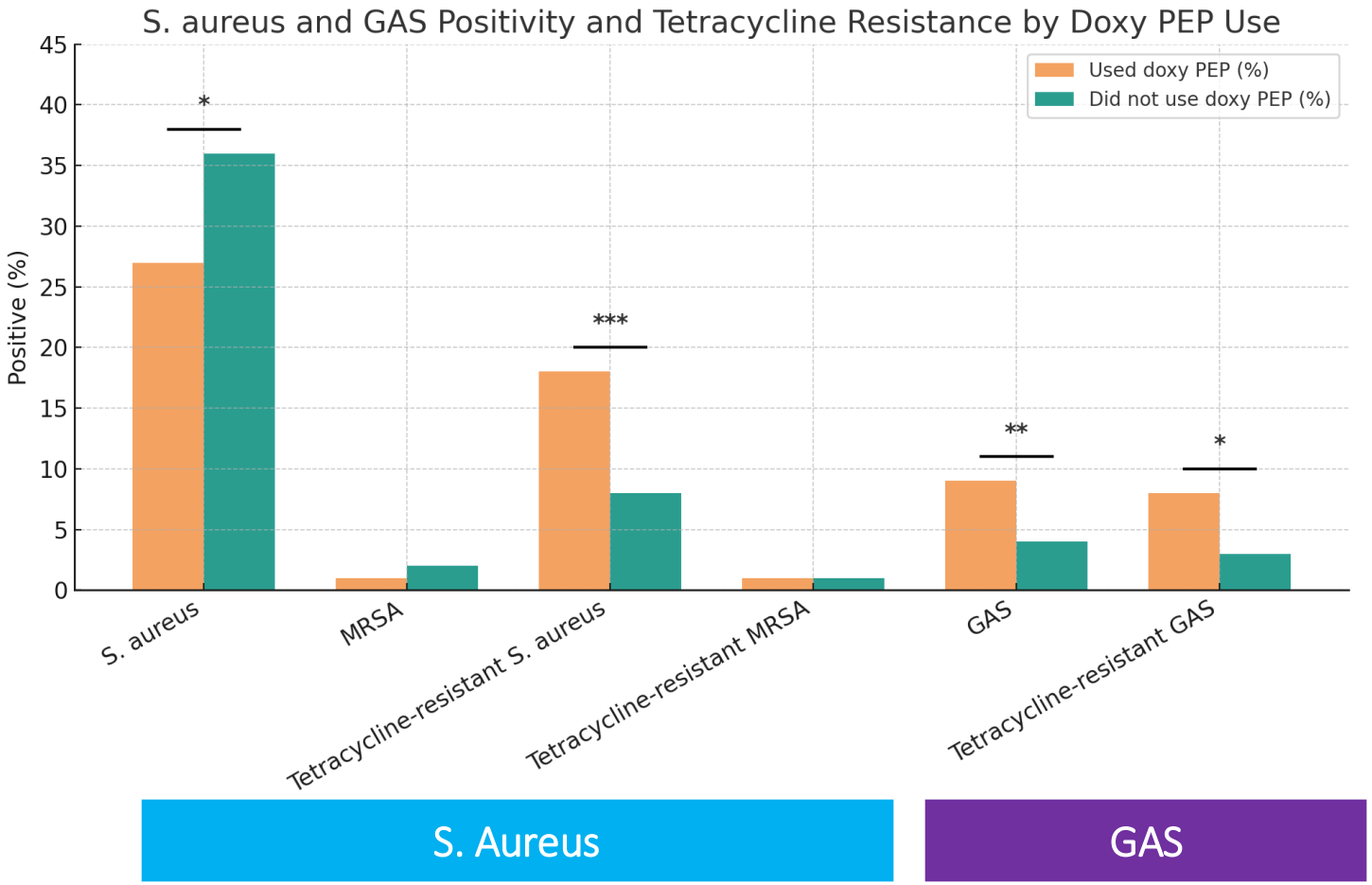
AMR in *S Aureus* & GAS



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Doxy-PEP use over 6 months minimally affected the taxonomic composition of the gut but…

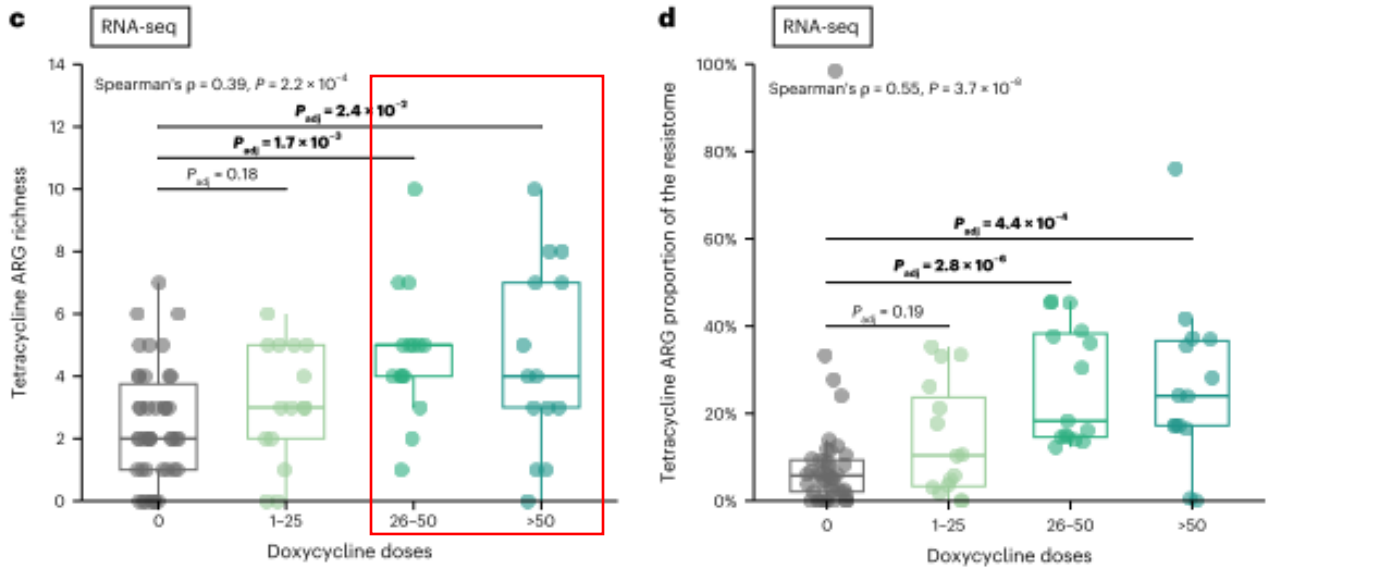

Fig. 4 | Impact of doxy-PEP use on tetracycline ARGs by number of doxycycline doses received for DNA-seq samples and RNA-seq samples. A test of trend was used to compare tetracycline ARG richness (**a**,**c**) and proportion of tetracycline ARG mass to resistome mass by number of doxycycline doses received (**b**,**d**) (DNA-seq: $n = 127$; RNA-seq: $n = 86$). *P* values were calculated using the two-sided Wilcoxon rank-sum test and adjusted for multiple comparisons. The two-sided Spearman's rank correlation test was used to calculate Spearman's ρ and *P* value. Box plot elements include a center line (median), box limits (upper and lower quartiles) and whiskers (1.5× IQR).

Chu et al, Nature Medicine, 2024

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Effect on Syphilis serological response

Correspondence

Doxycycline postexposure prophylaxis may delay seroconversion in incident syphilis

Angelo Roberto Raccagni [1], Elena Bruzzesi,[1] Antonella Castagna,[1,2] Silvia Nozza [1,2]

Ethics Committee of the IRCCS San Raffaele Scientific Institute, Milan, Italy (date of approval: 4 December 2017, protocol number 34). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; internally peer-reviewed.

Case Report

INTERNATIONAL JOURNAL OF STD & AIDS

DOXY do, or DOXY Don't? Syphilis and doxycycline post-exposure prophylaxis: A case report

International Journal of STD & AIDS
2024, Vol. 0(0) 1–3

DOI: 10.1177/09564624241308026
journals.sagepub.com/home/std
Sage

Omar Chircop[1], Courtney Jaggers[2], Martha Spiteri[3], Aaron Schembri[4] and Valeska Padovese[5]

STI&HIV2025 WORLD CONGRESS
July 26–30, 2025 · Montreal, Canada

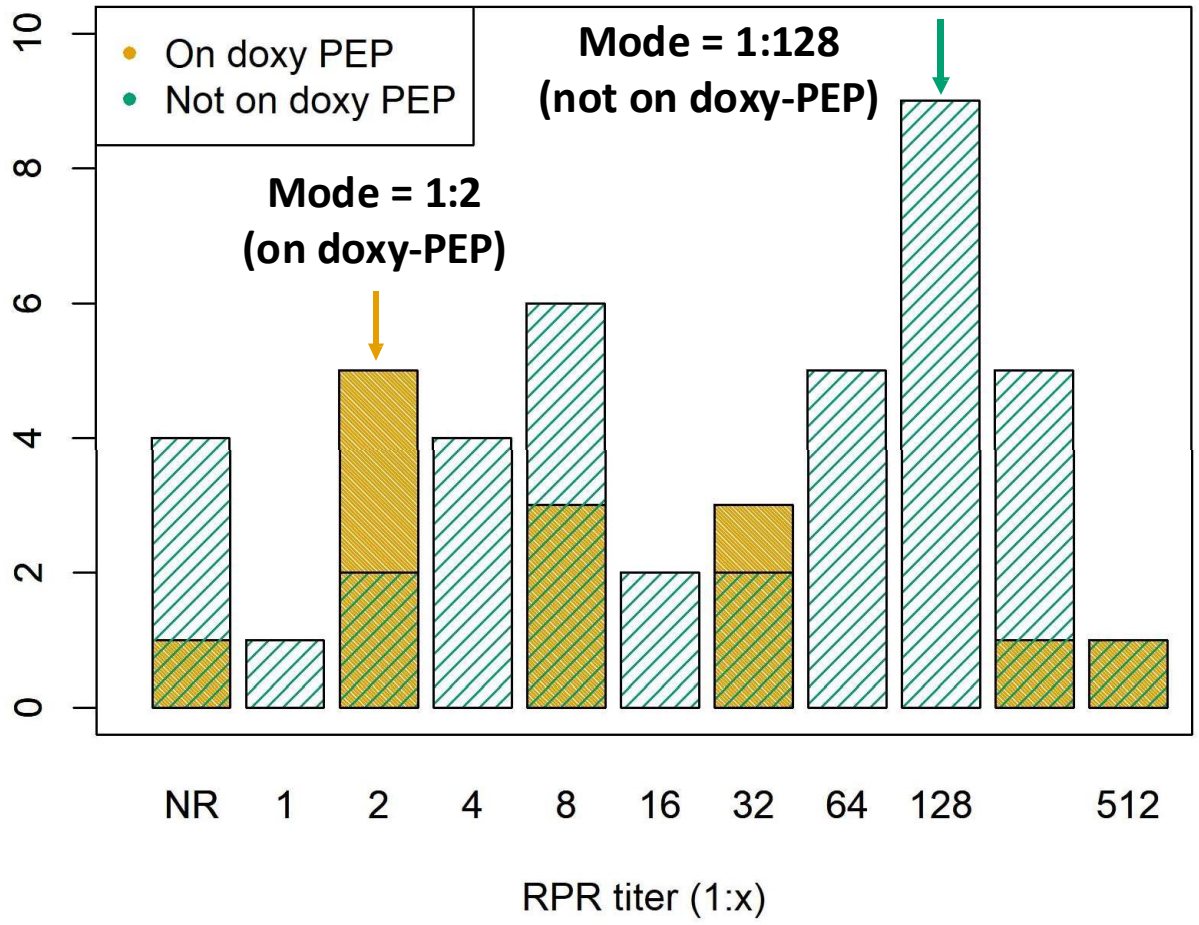
Results: New syphilis cases

59 syphilis cases in 56 patients	Doxy-PEP users	vs	Doxy-PEP non-users
	24%		71%

- Early latent was most common stage (56%)
- Higher proportion of primary & secondary (P&S) cases in doxy-PEP non-users (88%) vs users (12%)

STI&HIV2025 WORLD CONGRESS
July 26–30, 2025 · Montreal, Canada

Most common titer at ES diagnosis was 1:128 in non-users vs 1:2 in users



Conclusions

- DoxyPEP implementation is still debated in the world
- Real-world data seems to confirm the efficacy found in RCTs
- Evidence of increased AMR in *N gonorrhoeae*
  - Tetracycline resistance
  - Cephalosporine resistance?
- Evidence of increased resistance in other bacteria
- Evidence of increase AMR genes in the gut microbiome
- Risk of Syphilis mis-diagnosis/under-diagnosis

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Thank you!

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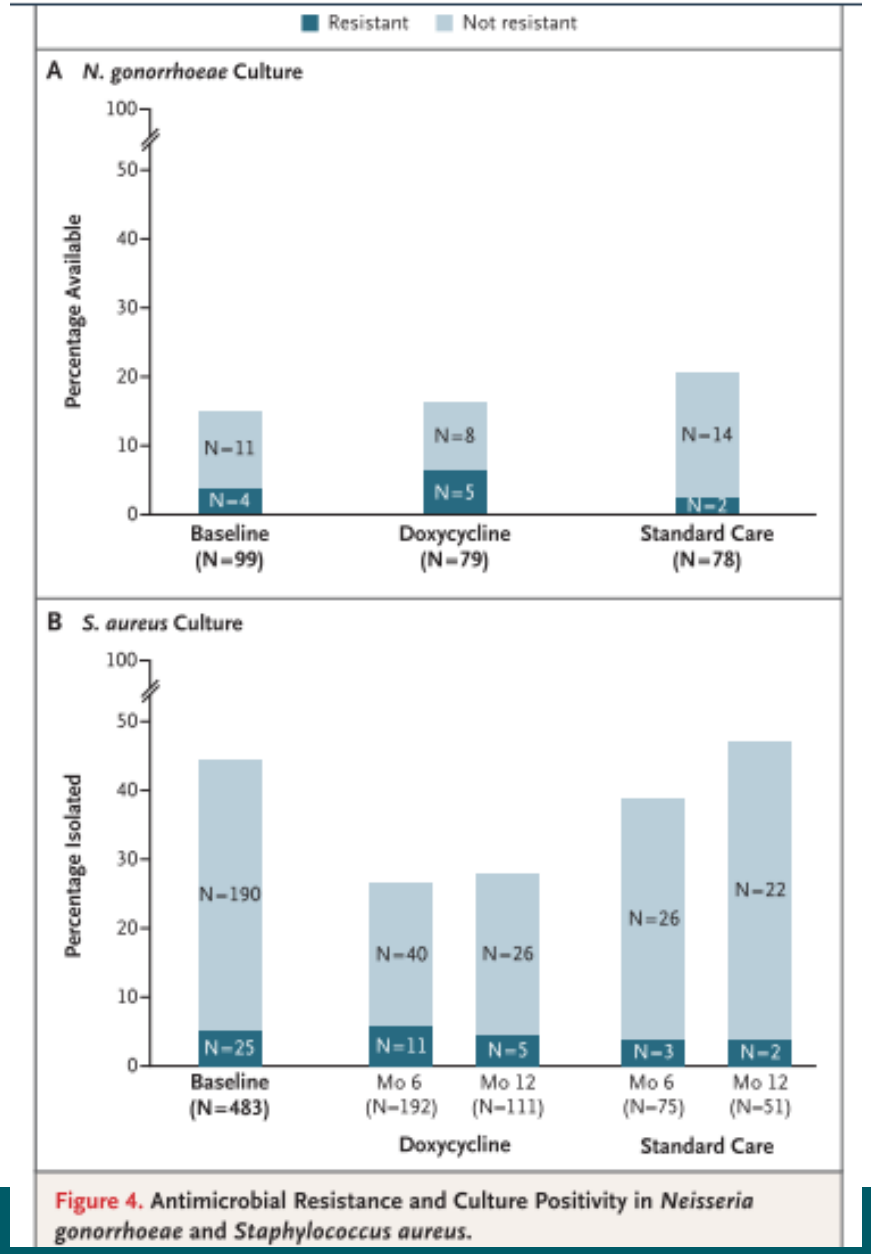

Figure 4. Antimicrobial Resistance and Culture Positivity in *Neisseria gonorrhoeae* and *Staphylococcus aureus*.

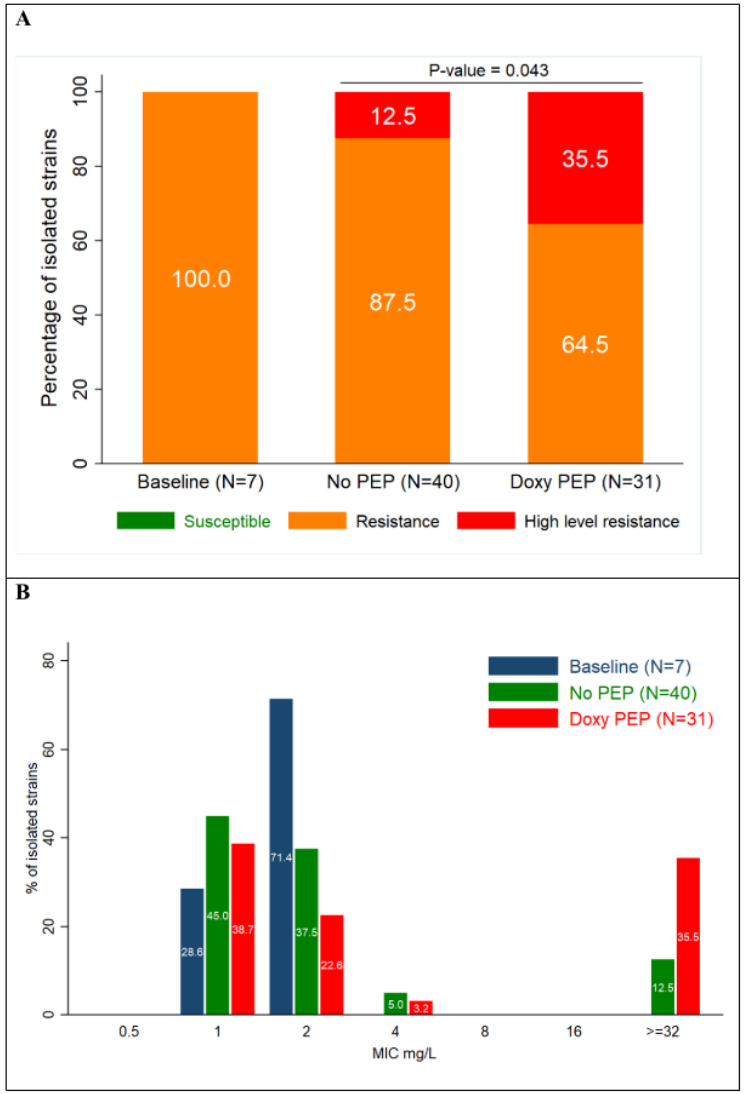

Figure S4. Percent of MRSA detected in throat swabs (A) and ESBL E. coli detected in recta swabs (B).